

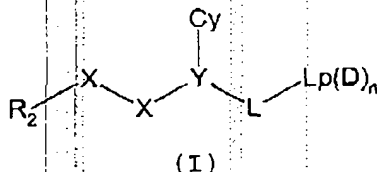
Serial No. 09/926,712  
Response to Office Action of July 30, 2003

# **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

1 (currently amended): A serine protease inhibitor compound of formula (I)



where R<sub>2</sub> represents

(i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>- or R<sub>1</sub>, and optionally substituted at the 6 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio; or

(ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>; and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;

~~(iii) isequinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;~~

~~(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;~~

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~~(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;~~

~~(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;~~

~~(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;~~

~~(viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;~~

~~(ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;~~

~~(x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;~~

~~(xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;~~

~~(xii) indol-2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>;~~

~~(xiii) indol-6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio and optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1</sub>; or~~

~~(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano,~~

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~~amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>,~~

~~with the proviso that R<sub>2</sub> cannot be aminoisquinolyl,~~

~~-X-X- is CONH each X independently is a C, N, O or S atom or a CO, CR<sub>1a</sub>, C(R<sub>1a</sub>)<sub>2</sub> or NR<sub>1a</sub> group, at least one X being C, CO, CR<sub>1a</sub> or C(R<sub>1a</sub>)<sub>2</sub>;~~

~~each R<sub>1a</sub> independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxy carbonyl, alkylaminocarbonyl, alkoxy carbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;~~

~~R<sub>1</sub> is as defined for R<sub>1a</sub>, provided that R<sub>1</sub> is not unsubstituted aminoalkyl;~~

~~L is CO, CH<sub>2</sub>NH, CONR<sub>1d</sub>(CH<sub>2</sub>)<sub>m</sub>, (CH<sub>2</sub>)<sub>m</sub>N(R<sub>1d</sub>)CO(CH<sub>2</sub>)<sub>m</sub>, (CH<sub>2</sub>)<sub>m+2</sub>, CO(CH<sub>2</sub>)<sub>m</sub>, (CH<sub>2</sub>)<sub>m</sub>CO, (CH<sub>2</sub>)<sub>m</sub>OC=O, (CH<sub>2</sub>)<sub>m</sub>O, CH=CH(CH<sub>2</sub>)<sub>m</sub>, SO<sub>2</sub>, SO<sub>2</sub>NR<sub>1d</sub>, SO<sub>2</sub>(CH<sub>2</sub>)<sub>m</sub>, (CH<sub>2</sub>)<sub>m</sub>SO<sub>2</sub> or (CH<sub>2</sub>)<sub>m</sub>SO<sub>2</sub>NR<sub>1d</sub> (where each m is independently 0 or 1 and R<sub>1d</sub> is hydrogen or an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group);~~

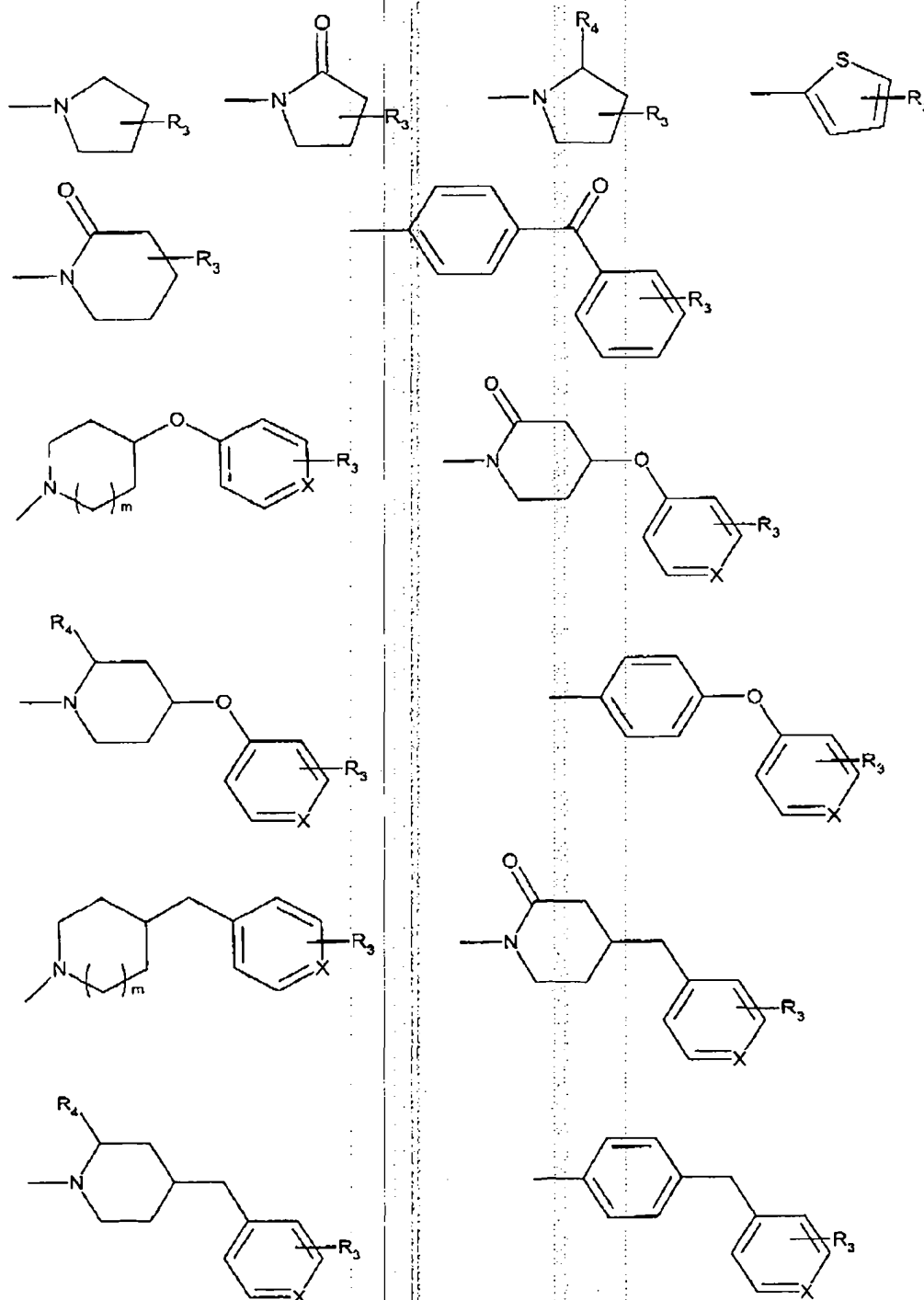
~~Y is a CH a nitrogen atom or a CR<sub>1b</sub> group;~~

~~Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group optionally substituted by groups R<sub>3a</sub> or phenyl optionally substituted by R<sub>3a</sub>;~~

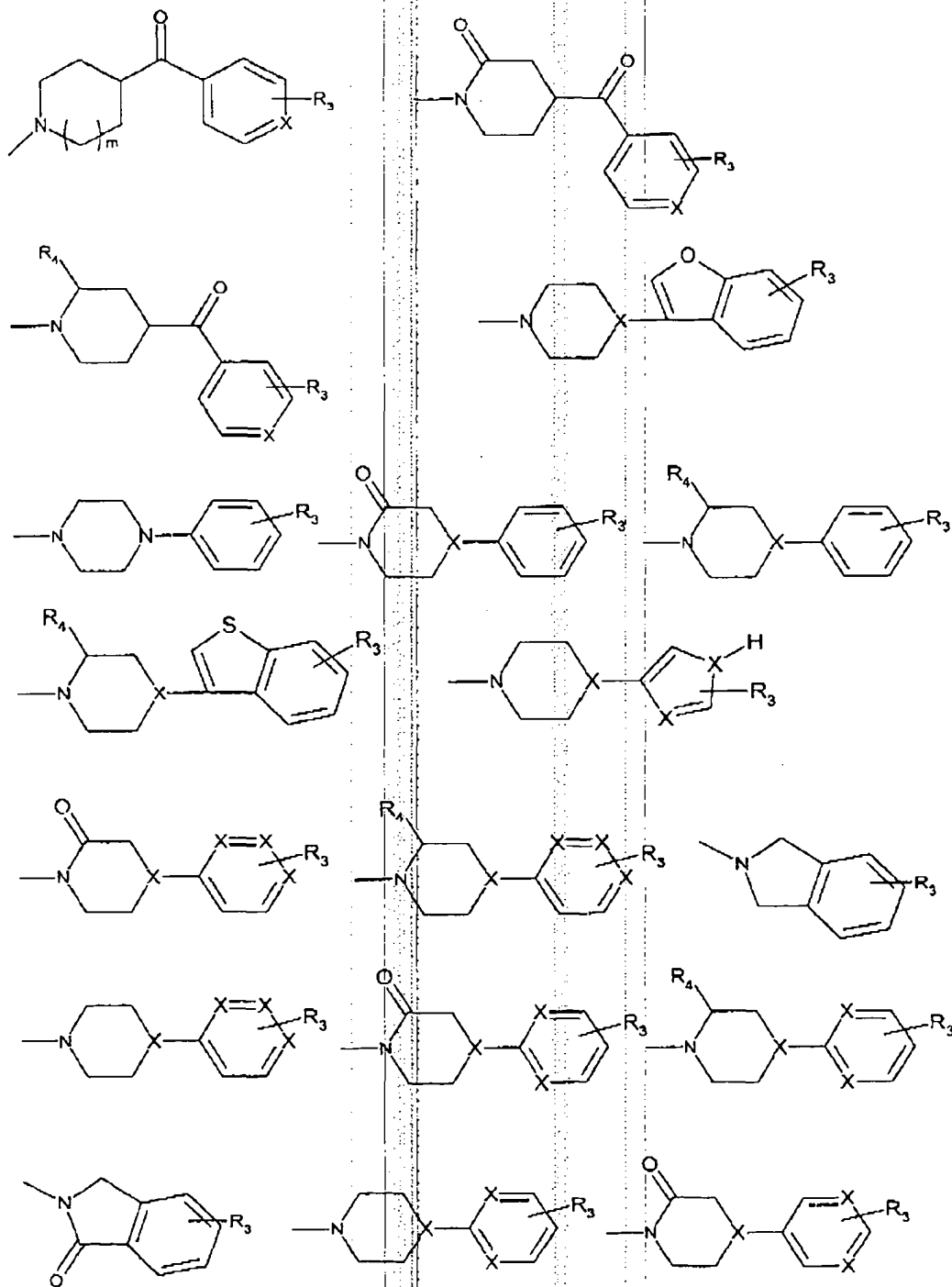
~~each R<sub>3a</sub> independently is R<sub>1c</sub>, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy and haloalkyl;~~

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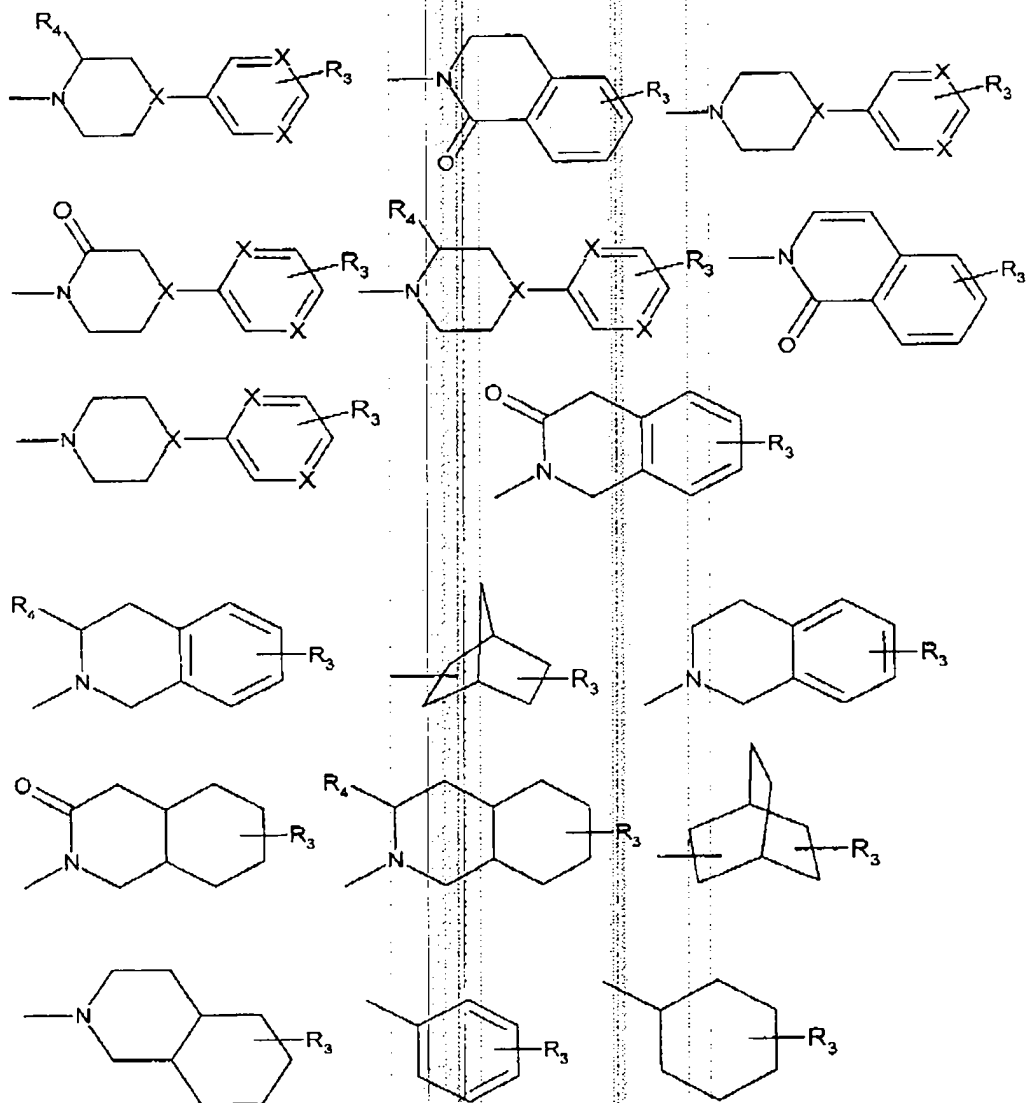
Lp is a lipophilic organic group selected from



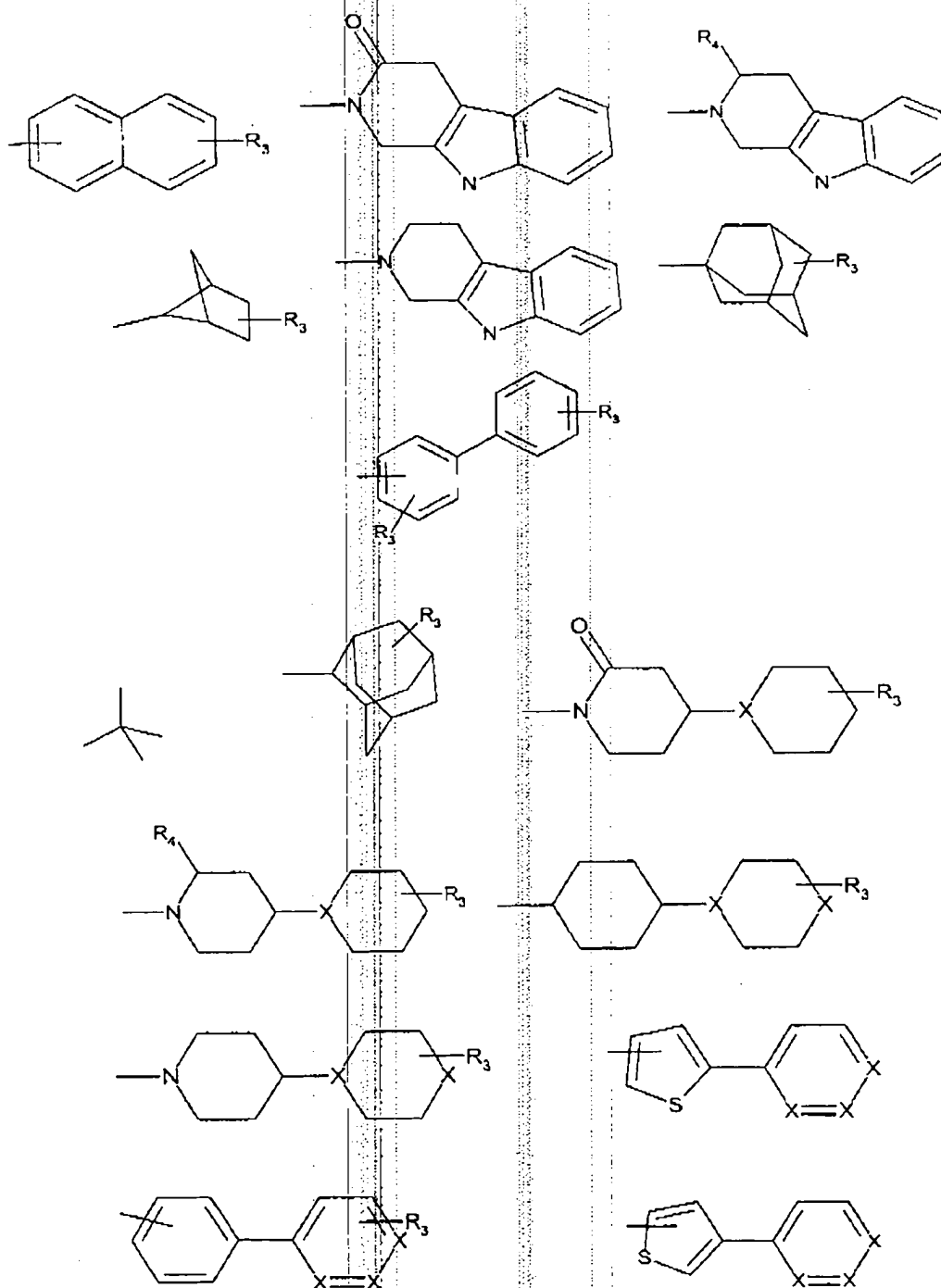
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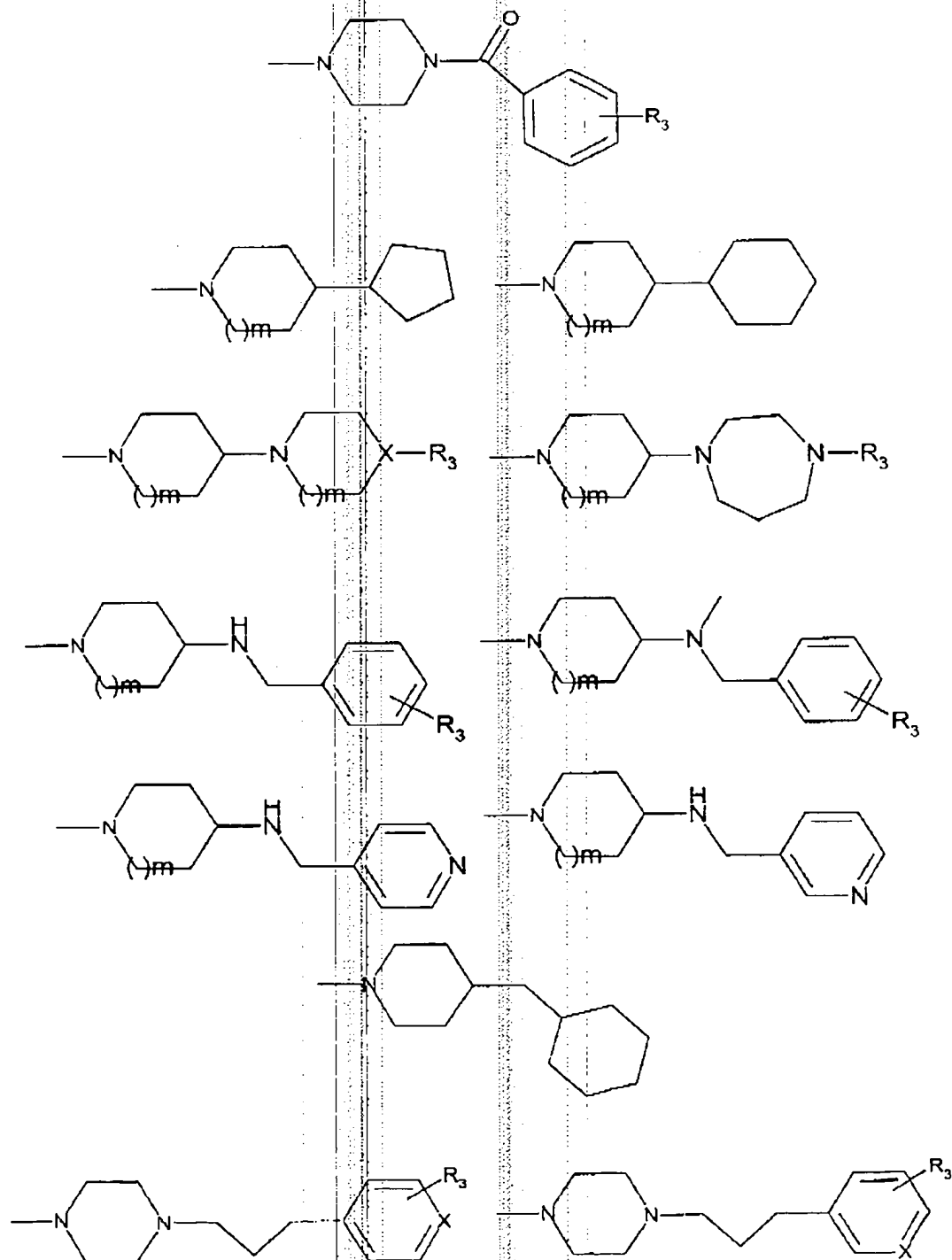
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wherein  $R_3$  is as defined for  $R_{3a}$ ;

$m$  represents 0 or 1;

$R_4$  represents hydrogen,  $(CH_2)_wCOOH$  or  $(CH_2)_wCONH_2$ ;

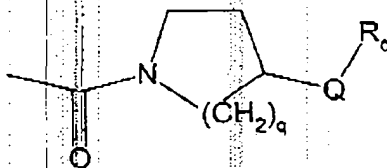
$w$  represents an integer from 0 to 4; and

$X$  represents CH or N;

$D$  is a hydrogen bond donor group; and  $n$  is 0;

or  $-L-Lp(D)_n$  is:

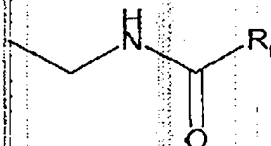
(i)



in which  $q$  is 1 or 2;

$Q$  is a direct bond; and  $R_q$  is piperidin-4-yl which may bear a  $C_{1-3}$ alkyl substituent at the 1-position; or  $R_q$  is  $NR_aR_b$  in which each of  $R_a$  and  $R_b$  independently is hydrogen or  $C_{1-3}$ alkyl; or one of  $R_a$  and  $R_b$  is hydrogen or methyl and the other of  $R_a$  and  $R_b$  is  $-CH_2-R_c$  or  $-CH_2-R_d$  in which  $R_c$  is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl,  $CONH_2$ ,  $SO_2NH_2$ , methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and in which  $R_d$  is isopropyl or cyclopentyl, or  $NR_aR_b$  is pyrrolidino, piperidino, morpholino, piperazino, or tetrahydro-1,4-diazepino in which a pyrrolidino or piperidino may be a 3,4-didehydro derivative and in which a pyrrolidino, piperidino, piperazino, or tetrahydro-1,4-diazepino may bear a methyl group at the 4-position;

(ii)



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in which  $R_t$  is phenyl (which phenyl may bear a fluoro, chloro,  $C_{1-4}$  alkyl, methoxy or methylsulphonyl substituent); or  
 (iii)



in which Het is a divalent 5 membered heteroaromatic group containing 1, 2 or 3 heteroatoms selected from O, N and S and having the two ring atoms at which it is connected separated by one ring atom;

$h$  is 0 or 1; and

$R_h$  is phenyl which may bear one or more  $R_3$  substituents;

and

$R_{1b}$ ,  $R_{1c}$  and  $R_{1j}$  are as defined for  $R_{1a}$ ,

or a physiologically tolerable salt thereof.

2 (canceled):

3 (canceled):

4 (canceled):

5 (canceled):

6 (currently amended): A compound as claimed in Claim 1, in which Y is a CH  $CR_{1b}$  group and has the conformation that would result from construction from a D- $\alpha$ -aminoacid  $NH_2-CH(Cy)-COOH$   ~~$NH_2-CR_{1b}(Cy)-COOH$~~  where the  $NH_2$  represents part of X-X.

7 (canceled):

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8 (currently amended): A compound as claimed in Claim 17, in which Cy represents an optionally  $R_{3a}$  substituted phenyl, ~~pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl~~ or cycloalkyl group.

9 (original): A compound as claimed in Claim 8, in which  $R_{3a}$  is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl,  $CONH_2$ ,  $CH_2CONH_2$ , acetyl amino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl.

10 (currently amended): A compound as claimed in Claim 1, in which Cy is phenyl, 4-aminophenyl, 4-amidophenyl, 4-(N-methyl)amidophenyl, 4-(N,N-dimethyl)amidophenyl, 2-chlorophenyl, 2-methylphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 4-hydroxyphenyl, 2-methoxyphenyl, 4-methoxyphenyl, 4-carboxyphenyl, 3-ethylsulphonylaminophenyl, ~~thien-2-yl, thien-3-yl, thiazol-4-yl, thiazol-5-yl, 2-methylthiazol-4-yl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, piperidin-4-yl, 1-methylpiperidin-4-yl~~, cyclohexyl or naphth-1-yl.

11 (canceled):

12 (currently amended): A compound as claimed in Claim 10~~11~~, in which L is CO, CONH,  $CH_2NHCO$  ~~and or~~  $CONHCH_2$ .

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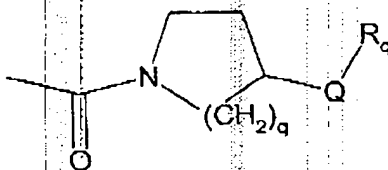
13. (canceled):

14. (canceled):

15 (canceled):

16 (previously presented): A compound as claimed in Claim 1, in which in  $-L-Lp(D)_n$  is:

(i)



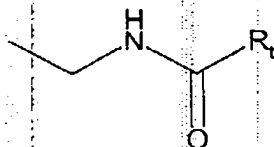
in which  $q$  is 1 or 2;

$Q$  is a direct bond; and  $R_q$  is piperidin-4-yl which may bear a  $C_{1-3}$ alkyl substituent at the 1-position; or  $R_q$  is  $NR_aR_b$  in which each of  $R_a$  and  $R_b$  independently is hydrogen or  $C_{1-3}$ alkyl; or one of  $R_a$  and  $R_b$  is hydrogen or methyl and the other of  $R_a$  and  $R_b$  is  $-CH_2-R_c$  or  $-CH_2-R_d$  in which  $R_c$  is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl,  $CONH_2$ ,  $SO_2NH_2$ , methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and in which  $R_d$  is isopropyl or cyclopentyl, or  $NR_aR_b$  is pyrrolidino, piperidino, morpholino, piperazino, or tetrahydro-1,4-diazepino in which a pyrrolidino or piperidino may be a 3,4-didehydro derivative and in which a pyrrolidino, piperidino, piperazino, or tetrahydro-1,4-diazepino may bear a methyl group at the 4-position;

(ii)

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in which  $R_t$  is phenyl (which phenyl may bear a fluoro, chloro,  $C_{1-4}$  alkyl, methoxy or methylsulphonyl substituent); or  
 (iii)



in which Het is a divalent 5 membered heteroaromatic group containing 1, 2 or 3 heteroatoms selected from O, N and S and having the two ring atoms at which it is connected separated by one ring atom;

$h$  is 0 or 1; and

$R_h$  is phenyl which may bear one or more  $R_3$  substituents.

17 (previously presented): A compound as claimed in Claim 16, in which

(i)  $q$  is 2, and

$R_q$  is piperidin-4-yl which may bear a (1-3C)alkyl substituent at the 1-position;

(iii)  $R_h$  is phenyl which may bear one or more  $R_3$  substituents independently selected from, for an ortho or a para substituent:  $C_{1-5}$  alkyl, fluoro, chloro, difluoromethyl, trifluoromethyl, methoxy, dimethylamino, methylsulphonyl, and  $C_{1-2}$  acyl, and for a meta substituent: fluoro, chloro and methyl.

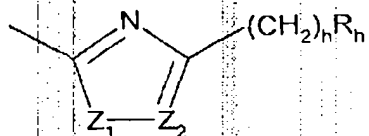
18 (previously presented): A compound as claimed in Claim 1, in which

$-L-Lp(D)_n$  is

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in which  $R_h$  is phenyl which may bear an ortho and/or a para substituent independently selected from, for an ortho: methyl, fluoro, chloro, methylsulphonyl and acetyl, and for a para substituent: methyl, fluoro, chloro, methoxy and dimethylamino;

$Z_1$  is S,  $Z_2$  is CH,  $h$  is 0; or

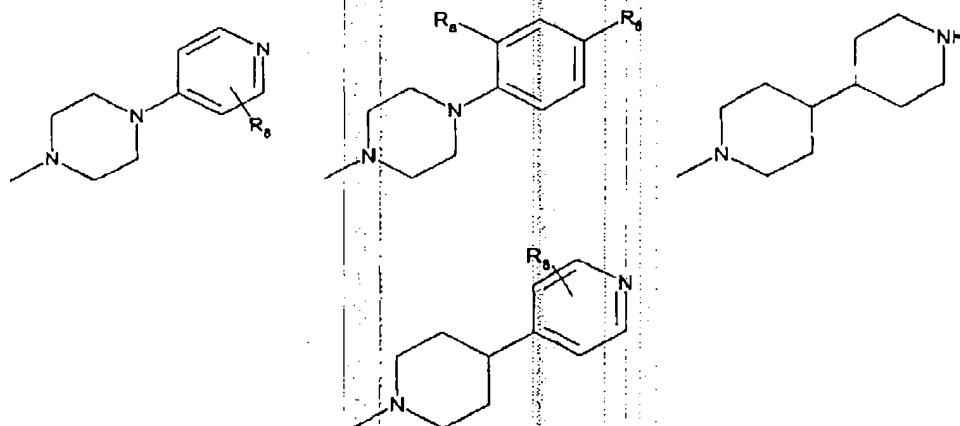
$Z_1$  is NH,  $Z_2$  is N,  $h$  is 1.

19 (previously presented): A compound as claimed in Claim 1, in which  $R_3$  is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, propyl, 2-propyl, butyl, 2-butyl, t-butyl, pentyl, 2-pentyl or 3-pentyl, isopropylaminomethyl, dimethylaminomethyl, diethylaminomethyl, dimethylaminoethyl, acetyl, hydroxymethyl, hydroxyethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminomethyl, aminocarbonyl, methylamino, dimethylamino, ethylamino, formylamino, acetylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, isopropylsulphonyl, methylsulphenyl, 1,2,4-triazol-2-yl, 1,2,4-triazol-4-yl, 1,2,3-triazol-4-yl, 1,3-imidazol-1-yl or 1,3-imidazol-4-yl, tetrazol-1-yl, tetrazol-5-yl; methylsulphonamido, ethylsulphonamido, propylsulphonamido, methylaminosulphonyl, ethylaminosulphonyl, propylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl and trichloromethyl.

20 (previously presented): A compound as claimed in Claim 1, in which  $L_p$  is selected from

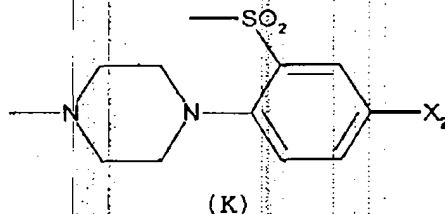
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where  $R_6$  represents H, OMe,  $SO_2Me$ , F, cyano, amido, amino,  $NO_2$ , Cl or OH.

21 (previously presented): A compound as claimed in Claim 1, in which  $L_p$  represents



wherein  $X_2$  is halo, hydrogen, amino, nitro or  $CONH_2$ .

22 (canceled):

23 (currently amended): A compound as claimed in Claim 1, in which  $R_2$  represents:

(i) phenyl optionally being substituted in the 3 and/or 4 position by fluoro, chloro, bromo, iodo, nitro, difluoromethoxy, trifluoromethoxy, amino, cyano, trifluoromethyl, methylthio, vinyl, carboxy, acetoxy,  $MeSO_2-$ , hydroxy, methoxy, ethoxy, methyl, methoxycarbonyl,

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methylamino, ethylamino or amido, and optionally substituted at the 6 position by amino, hydroxy, fluoro, methoxycarbonyl, cyano or aminomethyl; or

(ii) naphth-2-yl optionally substituted at the 6, position by hydroxy and optionally substituted at the 3 position by amino or hydroxy;

~~(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by chloro, bromo, amino, methyl or methoxy;~~

~~(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;~~

~~(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by methylthio, methyl or acetyl;~~

~~(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-5-yl, 3,3-dichloro-2-exo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;~~

~~(vii) benzothiazol-3-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;~~

~~(viii) pyrazol-2-yl substituted at the 5 position by methyl;~~

~~(ix) pyrid-2-yl optionally substituted at the 6 position by chloro;~~

~~(x) pyrid-3-yl optionally substituted at the 4 position by chloro;~~

~~(xi) benzofur-2-yl optionally substituted at the 3 position by chloro, methyl or methoxy, at the 5 or 6 position by methyl and at the 6 position by methoxy;~~

~~(xii) indol-2-yl optionally substituted on the indole nitrogen atom by methyl and optionally substituted at the 5 or 6 position by fluoro, chloro, bromo, methyl or methoxy;~~

~~(xiii) indol-6-yl substituted at the 5 position by chloro, fluoro or hydroxy and optionally substituted at the 3 position by chloro or methyl; or~~

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~~(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by fluoro, chloro or methyl, and optionally substituted at the 5 or 6 position by fluoro, chloro, methyl, hydroxy, or methoxy.~~

24 (canceled):

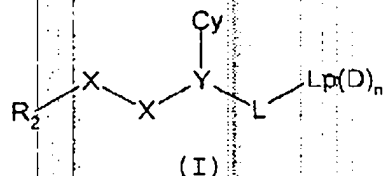
25 (canceled):

26 (canceled):

27 (original): A pharmaceutical composition, which comprises a compound as claimed in Claim 1 together with at least one pharmaceutically acceptable carrier or excipient.

28 (previously presented): A compound as claimed in Claim 23, in which R<sub>2</sub> represents phenyl substituted in the 4 position by chloro, amino, vinyl, methylamino, methyl or methoxy, optionally at the 3 position with amino or hydroxy, and optionally at the 6 position with amino or hydroxy.

29 (currently amended): A serine protease inhibitor compound of formula (I)



where R<sub>2</sub> represents

(i) phenyl optionally being substituted in the 3 and/or 4 position by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, MeSO<sub>2</sub>- or R<sub>1</sub>, and optionally substituted at the 6 position by

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amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio; or

(ii) naphth-2-yl optionally substituted at the 6 or 7 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$  and optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio;

~~(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;~~

~~(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;~~

~~(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;~~

~~(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxoindol-6-yl or 1-methyl-3-aminoindazol-5-yl;~~

~~(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;~~

~~(viii) pyrazol-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;~~

~~(ix) pyrid-2-yl optionally substituted at the 5 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;~~

~~(x) pyrid-3-yl optionally substituted at the 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or  $R_{1j}$ ;~~

~~(xi) benzofur-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amido, aminoalkyl, alkoxy or alkylthio and at the 5 or 6~~

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~~position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;~~

~~(xii) indol 2-yl optionally substituted on the indole nitrogen atom by alkyl and optionally substituted at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;~~

~~(xiii) indol 6-yl substituted at the 5 position by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amide, aminoalkyl, alkoxy or alkylthio and optionally substituted at the 3 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>; or~~

~~(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by amino, hydroxy, halo, alkyl, carboxy, cyano, amide, aminoalkyl, alkoxy or alkylthio and at the 5 or 6 position by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R<sub>1j</sub>;~~

~~with the proviso that R<sub>2</sub> cannot be aminoisquinolyl;~~

~~-X-X- represents -CONH- each X independently is a C, N, O or S atom or a CO, CR<sub>1a</sub>, C(R<sub>1a</sub>)<sub>2</sub> or NR<sub>1a</sub> group, at least one X being C, CO, CR<sub>1a</sub> or C(R<sub>1a</sub>)<sub>2</sub>;~~

~~each R<sub>1a</sub> independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;~~

~~R<sub>1</sub> is as defined for R<sub>1a</sub>, provided that R<sub>1</sub> is not unsubstituted aminoalkyl;~~

~~Y is a nitrogen atom or a CR<sub>1b</sub>CH group;~~

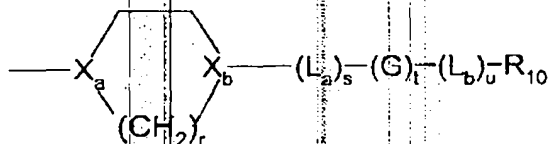
~~Cy is a saturated or unsaturated, mono or poly cyclic, homo- or heterocyclic group optionally substituted by groups R<sub>3a</sub> or phenyl optionally substituted by R<sub>3a</sub>;~~

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each  $R_{3a}$  independently is  $R_{1c}$ , amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy and haloalkyl;

$L_p$  is group of formula:



in which:

$r$  is 1 or 2;

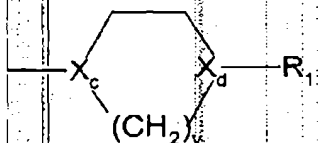
one of  $X_a$  and  $X_b$  is N and the other is CH or N provided that when  $r$  is 1,  $X_a$  and  $X_b$  are not both N;

$s$ ,  $t$  and  $u$  are each 0 or 1;

$L_a$  and  $L_b$  are each independently selected from a single bond,  $C=O$ ,  $O$  and  $NR_{1e}$ , in which  $R_{1e}$  is hydrogen or (1-6C)alkyl;

$G$  is (1-6C)alkanediyl; and

$R_{10}$  is (1-6C)alkyl, (3-6C)cycloalkyl which is unsubstituted or substituted by (1-6C)alkyl, indanyl, pyridyl, tetrahydropyranyl, tetrahydrothiopyranyl, phenyl which is unsubstituted or substituted by one or two  $R_3$  groups, pyrrolinyl, or a group of formula



in which  $v$  is 1, 2 or 3; one of  $X_c$  and  $X_d$  is N and the other is CH or N, provided that when  $v$  is 1,  $X_c$  and  $X_d$  are not both N; and  $R_{11}$  is hydrogen, (1-6C)alkyl or when  $X_d$  is CH, hydroxy(1-6C)alkyl; provided that when  $t$  is 0, the sum of  $s$

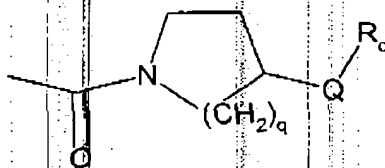
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and  $u$  is 1; when  $X_b$  is N,  $L_a$  is a bond or C=O; when  $X_c$  is N,  $L_b$  is a bond or C=O; when  $X_b$  and  $X_c$  are both N,  $t$  is 1; and when  $(L_a)_s-(G)_t-(L_b)$  represents an alkyl group and  $X_b$  and  $X_c$  both represent N, the alkyl group contains at least two chain carbon atoms,

where  $L$  is CO or  $CH_2CO$ , when  $X_a$  is N, or  $L$  is CONH,  $CONHCH_2$  or  $CH_2NHCO$  when  $X_a$  is CH;

but excluding compounds in which  $-L-Lp(D)_n$  is:

(i)



in which  $q$  is 1 or 2;

(a)  $Q$  is  $-O-$  or  $-NH-$ ; and  $R_q$  is  $R_c$ ; or

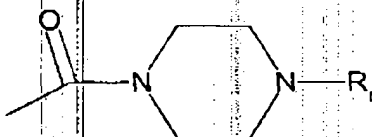
(b)  $Q$  is methylene; and  $R_q$  is  $NR_aR_b$ ;

each of  $R_a$  and  $R_b$  independently is hydrogen or  $C_{1-3}$ alkyl; or one of  $R_a$  and  $R_b$  is hydrogen or methyl and the other of  $R_a$  and  $R_b$  is  $-CH_2-R_c$  or  $-CH_2-R_d$  in which  $R_c$  is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl,  $CONH_2$ ,  $SO_2NH_2$ , methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and in which  $R_d$  is isopropyl or cyclopentyl, or  $NR_aR_b$  is pyrrolidino, piperidino, morpholino, piperazino, or tetrahydro-1,4-diazepino in which a pyrrolidino or piperidino may be a 3,4-didehydro derivative and in which a pyrrolidino, piperidino, piperazino, or tetrahydro-1,4-diazepino may bear a methyl group at the 4-position;

(ii)

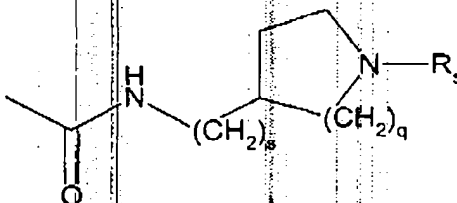
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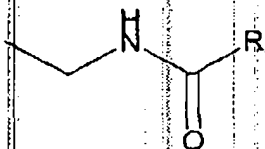
in which  $R_f$  is  $-(CH_2)_c-R_c$ ,  $-CHReR_f$ ,  $-CH_2-CHReR_f$ , or  $R_g$  in which  $c$  is 1 or 2 and  $R_c$  is defined as above; each of  $R_e$  and  $R_f$  independently is hydrogen or  $C_{1-3}$ alkyl; or  $CHReR_f$  is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent), or indan-2-yl; and  $R_g$  is 2-methylsulphonylphenyl which may bear a 4-fluoro substituent or  $R_g$  is  $\lambda^6$ -1,1-dioxobenzo[b]thiophen-7-yl;

(iii)

in which  $q$  is 1 or 2; $s$  is 0 or 1; and

$R_s$  is  $-(CH_2)_c-R_c$ ,  $-CHReR_f$ , or  $-CH_2-CHReR_f$  each of which is defined as above; or

(iv)



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in which  $R_c$  is piperidin-4-yl, piperidin-3-yl or pyrrolidin-3-yl, any of which may bear a  $C_{1-3}$  alkyl substituent at the 1-position;

D is a hydrogen bond donor group; and n is 0;

and

~~$R_{1b}$ ,  $R_{1c}$  and  $R_{1j}$~~  are as defined for  $R_{1a}$ ,  
or a physiologically tolerable salt thereof.

30 (canceled):

31 (canceled):

32 (currently amended): A compound as claimed in Claim 29, in which Y is a CH  ~~$CR_{1b}$~~ -group and has the conformation that would result from construction from a D- $\alpha$ -aminoacid  $NH_2-CH(Cy)-COOH$   ~~$NH_2-CR_{1b}(Cy)-COOH$~~  where the  $NH_2$  represents part of X-X.

33 (canceled):

34 (currently amended): A compound as claimed in Claim 33, in which Cy represents an optionally  $R_{3a}$  substituted phenyl, ~~pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl~~ or cycloalkyl group.

35 (previously presented): A compound as claimed in Claim 34, in which  $R_{3a}$  is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl,  $CONH_2$ ,  $CH_2CONH_2$ , acetyl amino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro,

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thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl.

36 (currently amended): A compound as claimed in Claim 29, in which Cy is phenyl, 4-aminophenyl, 4-amidophenyl, 4-(N-methyl)amidophenyl, 4-(N,N-dimethyl)amidophenyl, 2-chlorophenyl, 2-methylphenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 4-hydroxyphenyl, 2-methoxyphenyl, 4-methoxyphenyl, 4-carboxyphenyl, 3-ethylsulphonylaminophenyl, ~~thien 2-yl, thien 3-yl, thiazol 4-yl, thiazol 5-yl, 2-methylthiazol 4-yl, pyrid 2-yl, pyrid 3-yl, pyrid 4-yl, piperidin 4-yl, 1-methylpiperidin 4-yl~~, cyclohexyl or naphth-1-yl.

37 (previously presented): A compound as claimed in Claim 29, in which R<sub>3</sub> is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, propyl, 2-propyl, butyl, 2-butyl, t-butyl, pentyl, 2-pentyl or 3-pentyl, isopropylaminomethyl, dimethylaminomethyl, diethylaminomethyl, dimethylaminoethyl, acetyl, hydroxymethyl, hydroxyethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminomethyl, aminocarbonyl, methylamino, dimethylamino, ethylamino, formylamino, acetylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, isopropylsulphonyl, methylsulphenyl, 1,2,4-triazol-2-yl, 1,2,4-triazol-4-yl, 1,2,3-triazol-4-yl, 1,3-imidazol-1-yl or 1,3-imidazol-4-yl, tetrazol-1-yl, tetrazol-5-yl; methylsulphonamido, ethylsulphonamido, propylsulphonamido, methylaminosulphonyl, ethylaminosulphonyl,



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propylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl and trichloromethyl.

38 (currently amended): A compound as claimed in Claim 29, in which R<sub>2</sub> represents:

(i) phenyl optionally being substituted in the 3 and/or 4 position by fluoro, chloro, bromo, iodo, nitro, difluoromethoxy, trifluoromethoxy, amino, cyano, trifluoromethyl, methylthio, vinyl, carboxy, acetoxy, MeSO<sub>2</sub>-, hydroxy, methoxy, ethoxy, methyl, methoxycarbonyl, methylamino, ethylamino or amido, and optionally substituted at the 6 position by amino, hydroxy, fluoro, methoxycarbonyl, cyano or aminomethyl; or

(ii) naphth-2-yl optionally substituted at the 6, position by hydroxy and optionally substituted at the 3 position by amino or hydroxy;

~~(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by chloro, bromo, amino, methyl or methoxy;~~

~~(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;~~

~~(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by methylthio, methyl or acetyl;~~

~~(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;~~

~~(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;~~

~~(viii) pyrazol-2-yl substituted at the 5 position by methyl;~~

~~(ix) pyrid-2-yl optionally substituted at the 6 position by chloro;~~

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~~(x) pyrid-3-yl optionally substituted at the 4 position by chloro;~~

~~(xi) benzofur-2-yl optionally substituted at the 3 position by chloro, methyl or methoxy, at the 5 or 6 position by methyl and at the 6 position by methoxy;~~

~~(xii) indol-2-yl optionally substituted on the indole nitrogen atom by methyl and optionally substituted at the 5 or 6 position by fluoro, chloro, bromo, methyl or methoxy;~~

~~(xiii) indol-6-yl substituted at the 5 position by chloro, fluoro or hydroxy and optionally substituted at the 3 position by chloro or methyl; or~~

~~(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by fluoro, chloro or methyl, and optionally substituted at the 5 or 6 position by fluoro, chloro, methyl, hydroxy, or methoxy.~~

39 (previously presented): A compound as claimed in Claim 38, in which R<sup>2</sup> is phenyl substituted in the 4 position by chloro, amino, vinyl, methylamino, methyl or methoxy, optionally at the 3 position with amino or hydroxy, and optionally at the 6 position with amino or hydroxy.

40 (canceled):

41 (previously presented): A pharmaceutical composition, which comprises a compound as claimed in Claim 29 together with at least one pharmaceutically acceptable carrier or excipient.

42 (new): A compound as claimed in Claim 1, which is selected from:

1-(3-Amino-4-chlorobenzoyl-D-phenylglyciny)-4-(4-fluoro-2-methylsulphonylphenyl)piperazine;

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1-(3-Amino-4-chlorobenzoyl-D-phenylglyciny1)-1'-methyl-4,4'-  
bispiperidine;

1-(3-Amino-4-chlorobenzoyl-D-phenylglyciny1)-4-(2-  
methylsulphonylphenyl)piperazine;  
and physiologically tolerable salts thereof.

43 (new): A pharmaceutical composition, which comprises a  
compound as claimed in Claim 42 together with at least one  
pharmaceutically acceptable carrier or excipient.